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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,567	01/06/2000	A. Guruaj Rao	5718-16B	1859

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EXAMINER	
KALLIS, RUSSELL	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/478,567	RAO ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): 112 1st new matter and 112 2nd.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-3,5-12 and 14-20*.

   Claim(s) withdrawn from consideration: _____.

8. ☒ The drawing correction filed on *06 January 2000* is a)☐ approved or b)☒ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 2. NOTE: Applicant has amended the claims to recite "an increase to at least" that broadens the claim and would require further search and consideration. Further, Applicant has not submitted a proper amendement in that the addition of 'binds" to the next to last, and last lines of Claims 1 and 8 respectively were not underlined

Continuation of 5. does NOT place the application in condition for allowance because: The rejection under 35 U.S.C. 112, first paragraph, writen description and enablement, and under 35 U.S.C. 102 and 103 is maintained for reasons of record. The claims read upon any engineered protein of unspecified identity designed to have an increase in essential amino acid content of at least 5% that binds in any fashion to another unspecified or undefined protein of unspecified identity that binds in any fashion to VSP alpha or VSP beta under non-specified conditions. Further, the drawings remain objected to for reasons of record, and in addition, in figure 3B, VSPM1 should be VSPM10.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

DETAILED ACTION

Final

Claims 1-3, 5-12, and 14-20 are examined. Claims 4 and 13 are cancelled.

The rejection of Claims 18-20 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of Applicant's amendments.

Specification

The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figures 1, 2, and 4 describe VSP sequences that each must have a sequence identifier. Correction is required.

Claim Rejections - 35 USC § 112

Claims 1-3, 5-12 and 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The added claimed material which is not supported by the original disclosure is as follows: Newly amended Claims 1 and 8 recite "by at least one essential amino acid residue" while the specification only supports "significantly higher levels of methionine in lines 26-27 of page 2; "the proteins can be designed to be enriched in essential amino acids . . . relative to average levels of such amino acids" in lines 27-30 on page 3, and an increased essential amino acid content within the protein of at least about 5%, 10%, 20% or 40% of the total amino acid

content on page 7, lines 25-32 and page 8, line 1. Further, there is no support for "by at least one essential amino acid residue" in the originally filed claims of Application 08/988,015 filed 12/10/97. Support cannot be found on the pages Applicant indicated. Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant asserts that the specification provides exemplary nucleotide and amino acid sequences as well as guidance regarding the evaluation of the functional limitations of the claims (response page 8). The claims are drawn to nucleic acid molecules encoding engineered proteins having increased essential amino acid content. Applicant does not describe a representative number of exemplary nucleic acid molecules that define the genus of sequence having increased essential amino acid content as broadly claimed. There is insufficient relevant identifying characteristics to allow one of skiil in the art to predictably determine the structure of other nucleic acid molecules absent further guidance.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserts that the specification provides exemplary guidance for evaluation of the functional limitations of the claims (response page 9). Applicant teaches methionine enriched variant VSPβ-10 binding to wild type VSPβ specific antibodies (page 19) which only suggest that VSPβ-met10 may be correctly folded in an *E. coli* secretion system as stated by Applicant in the specification on page 20, lines 1-2. This does not meet required level of certainty as recited in the limitation of Claims 1 and 8 "retains the conformation of the native protein and therefore binds". Further, Applicant has not addressed the Examiner's statements in the enablement rejection directed towards the limitations of monoclonal antibodies in discriminating against non-native or non-corresponding VSPβ variants. Moreover, the results Applicant recites on page 19 of the specification do not indicate any background binding as relative control. Furthermore, no guidance is provided for making an engineered protein having an altered amino acid composition that would bind to a modified protein that binds to a native protein. It is uncertain which alteration would be compatible with the other alterations and how one would assay for productive binding. Nonetheless, undue experimentation would be required to make, clone, and express a multitude of non-exemplified variants of a nucleic acid molecule encoding a protein engineered for an increase in the level of essential amino acids, that binds with an antibody or protein molecule that also binds with a native form of the engineered protein and would require one of skill in the art to test in a myriad of non-exemplified plants for expression. Therefore, the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-12, and 14-20 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, and throughout the claims, "at least about" is indefinite because it sets a lower limit but "about" can be below that limit. Therefore, the metes and bounds are unclear.

At Claim 1 and 8, "capable of binding" is indefinite. It is unclear if the binding is specific or non-specific or under what conditions binding would occur. It is suggested that "capable of" be deleted.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. In the present instance, Claims 1 and 8 recite the broad recitation "an engineered protein comprising an amino acid sequence which differs from the amino acid sequence of a native protein by at least one essential amino acid residue", and the claims also recite "wherein said engineered protein has an altered amino acid composition in comparison to said native protein, wherein said altered amino acid composition comprises an increase in essential amino acid content to be at least about 5%", which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5-11, 14 and 17-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Jung R. *et al.* WO 97/35023 published September 25, 1997.

The claims read on any transgenic plant transformed with any polynucleotide altered to encode a protein engineered to have increased essential amino acid changes (i.e. methionine and cysteine) and that differs from the amino acid sequence of a native VSPα or VSPβ protein by at least one essential amino acid residue, and that binds in any fashion with any antibody or any protein, as does the corresponding native VSPα or VSPβ protein.

The claims are broadly drawn to soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Jung teaches an isolated soybean 2S Albumin protein cDNA (Example 2 page 32); an isolated soybean 2S Albumin protein cDNA engineered (Albumin 1/3) to have 13.14% lysine and 12.4% methionine and cysteine (Example 3 pages 35-36); transformation of soybean plants transformed with cDNA encoding modified soybean 2S Albumin, a vegetative seed protein, said engineered peptides and seeds thereof (Example 4 pages 37-42); and preparation of Albumin specific antibodies that bind to both native and engineered soybean 2S Albumin proteins (Example 4 pages 42-43). Thus, the reference teaches all the limitations of Claims 1-3, 5-11, 14 and 17-18.

Claims 1-3, 5-12, 15-16 and 18-20 remain rejected under 35 U.S.C. 102(e) as being anticipated by Tarczynski M. *et al.* U.S. Patent 6,080,913 filed September 25, 1996.

The claims read on any transgenic plant transformed with any polynucleotide altered to encode a protein engineered to have increased essential amino acid changes (i.e. methionine and cysteine) and that differs from the amino acid sequence of a native VSPα or VSPβ protein by at least one essential amino acid residue, and that binds in any fashion with any antibody or any protein, as does the corresponding native VSPα or VSPβ protein.

The claims are drawn to maize and soybean plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have at least one essential amino acid increased to 10% of total amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

Tarczynski teaches transformation of maize with an engineered cDNA from barley encoding a high lysine derivative of alpha-hordothione and plants having 20% or more of the target amino acid (see Claims 1, 9-11, 14-15, 17 and 19-22), a seed vegetative storage protein, targeted to the seed (Example III columns 13-14); and an endoplasmic reticulum targeting sequence KDEL for retention in the ER of maize that interacts with the proteins of the ER as do the corresponding native maize proteins. Thus the reference teaches all the limitations of Claims 1-3, 5-12, 15-16 and 18-20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-11, 14-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jung R. *et al.* WO 97/35023 published September 25, 1997 in view of Gordon-Kamm *et al.* The Plant Cell, July 1990; Vol. 2; pp. 603-608.

The claims are drawn to soybean and maize plants transformed with a nucleic acid molecule encoding a vegetative storage protein engineered to have an essential amino acid increased to 10% of total protein amino acid content compared to the native protein wherein the engineered protein binds to a molecule that binds to the native form of the protein.

The teachings of Jung are discussed supra.

Jung does not teach Maize transformation.

Gordon-Kamm *et al.* teach transformation of maize (pages 615-616).

It would have been obvious at the time of Applicant's invention to modify the invention of Jung to include a method for transformation of maize. One of skill in the art would have been motivated by the knowledge common in the art that the method of maize transformation as taught by Gordon-Kamm *et al.* is valuable for genetic engineering of plants to enhance the amino acid profile of a plant by expression of an engineered protein as taught by Jung *et al.* are and given the success of Gordon-Kamm in the expression of exogenous genes in Maize and Jung in expression of amino acid enhanced peptides in soybean, one would have had a reasonable expectation of success of expressing genes encoding amino acid enhanced peptides in transformed maize plants and plant cells.

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
March 30, 2004